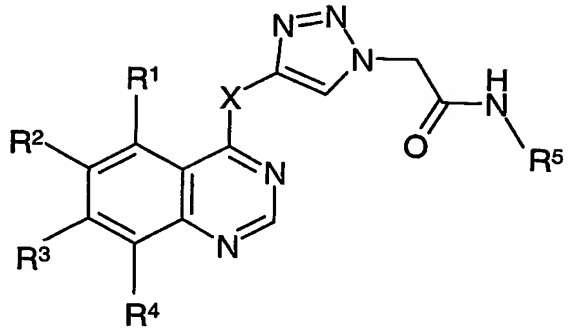
CLAIMS

What we claim is:

1. A compound of formula (I)



or a salt, ester or prodrug thereof;

where:

X is O or NR^6;

$\mathbf{R^6}$ is hydrogen or C_{1-4}alkyl;

$\mathbf{R^1}$ is hydrogen, halo, or $-X^1R^{11}$;

$\mathbf{X^1}$ is a direct bond, $-CH_2=CH_2-$, -O-, -NH-, $-N(C_{1-6}alkyl)-$, -C(O), -C(O)O, -OC(O)-, -NHC(O)-, $-N(C_{1-6}alkyl)C(O)-$, -C(O)NH or $-C(O)N(C_{1-6}alkyl)-$;

$\mathbf{R^{11}}$ is hydrogen, or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl which group is optionally substituted by 1 or 2 substituents independently selected from halo, hydroxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, $-NR^9R^{10}$, $-C(O)R^9$, $-C(O)NR^9R^{10}$ and $-C(O)OR^9$;

$\mathbf{R^2}$ is hydrogen, halo, nitro, cyano or $-X^2R^{12}$;

$\mathbf{X^2}$ is a direct bond, -O-, -NH-, $-N(C_{1-6}alkyl)-$, -OC(O)- or -C(O)O-;

$\mathbf{R^{12}}$ is hydrogen, or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, aryl, arylC_{1-4}alkyl, arylC_{2-4}alkenyl, arylC_{2-4}alkynyl, heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl, which group is optionally substituted by 1, 2 or 3 substituents independently selected from, halo, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, $-NR^{15}R^{16}$, $-NHC(O)NR^{15}R^{16}$, $-C(O)R^{15}$ and $-C(O)OR^{15}$;

$\mathbf{R^3}$ is hydrogen, halo or $-X^3R^{13}$;

$\mathbf{X^3}$ is a direct bond, $-CH_2=CH_2-$, -O-, -NH-, $-N(C_{1-6}alkyl)-$, -C(O)-, -C(O)O-, -OC(O)-, -NHC(O)-, $-N(C_{1-6}alkyl)C(O)-$, -C(O)NH- or $-C(O)N(C_{1-6}alkyl)-$;

R^{13} is hydrogen, or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, aryl, arylC_{1-4}alkyl, arylC_{2-4}alkenyl, arylC_{2-4}alkynyl, heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl which group is optionally substituted by 1 or 2 substituents independently selected from $-NR^7R^8$, $-C(O)NR^7R^8$, halo, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, hydroxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl;

R^7 and R^8 are independently selected from hydrogen, heterocyclyl, heterocyclylC_{1-4}alkyl, C_{1-4}alkylheterocyclylC_{1-4}alkyl, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-4}alkoxyC_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{3-6}cycloalkyl, hydroxyC_{1-4}alkylC_{3-6}cycloalkyl, hydroxyC_{1-4}alkylC_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{3-6}cycloalkylC_{1-4}alkyl, C_{1-4}alkoxyC_{3-6}cycloalkyl, C_{1-4}alkoxyC_{3-6}cycloalkylC_{1-4}alkyl, haloC_{1-6}alkyl, haloC_{3-6}cycloalkyl, haloC_{3-6}cycloalkylC_{1-4}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyanoC_{1-4}alkyl, aminoC_{1-6}alkyl, C_{1-4}alkylaminoC_{1-6}alkyl, bis(C_{1-4}alkyl)aminoC_{1-6}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl;

or R^7 and R^8 together with the nitrogen to which they are attached form a heterocyclic ring which ring is moncyclic or bicyclic and comprises 4 to 7 ring atoms of which one is nitrogen and of which another is optionally selected from N, NH, O, S, SO and SO_2, and which ring is optionally substituted on carbon or nitrogen by 1 or 2 substituents independently selected from C_{1-4}alkyl, hydroxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl, and where a ring $-CH_2-$ is optionally replaced with $-C(O)-$;

R^4 is selected from hydrogen, halo or $-X^4R^{14}$;

X^4 is a direct bond, -O-, -NH- or $-N(C_{1-6}alkyl)-$;

R^{14} is selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl and C_{2-6}alkynyl;

R^5 is aryl or heteroaryl optionally substituted by 1, 2 or 3 substituents independently selected from halo, hydroxy, cyano, nitro, amino, C_{1-4}alkylamino, bis(C_{1-4}alkyl)amino, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, $-C(O)NHR^{17}$, $-NHC(O)R^{18}$, $-SR^{17}$, $-S(O)R^{17}$ and $-S(O)OR^{17}$;

R^9, R^{10}, R^{15} and R^{16} are independently selected from hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{1-6}alkyl, haloC_{1-6}alkyl, aminoC_{1-6}alkyl, C_{1-4}alkylaminoC_{1-6}alkyl and bis(C_{1-4}alkyl)aminoC_{1-6}alkyl;

or R^9 and R^{10} together with the nitrogen to which they are attached form a heterocyclic ring which ring is monocyclic or bicyclic and comprises 4 to 7 ring atoms of which one is nitrogen and of which another is optionally selected from N, NH, O, S, SO and SO_2, and which ring is optionally substituted on carbon or nitrogen by 1 or 2 substituents independently selected from C_{1-4}alkyl, hydroxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl, and where a ring $-CH_2-$ is optionally replaced with $-C(O)-$;

R^{17} and R^{18} are independently selected from hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, C_{2-4}alkenyl and C_{2-4}alkynyl.

2. A compound according to claim 1 or a salt, ester or prodrug thereof wherein X is NH.

3. A compound according to claim 1 or a salt, ester or prodrug thereof wherein R^4 is hydrogen.

4. A compound according to claim 1 or a salt, ester or prodrug thereof wherein R^5 is aryl optionally substituted by 1 or 2 halo.

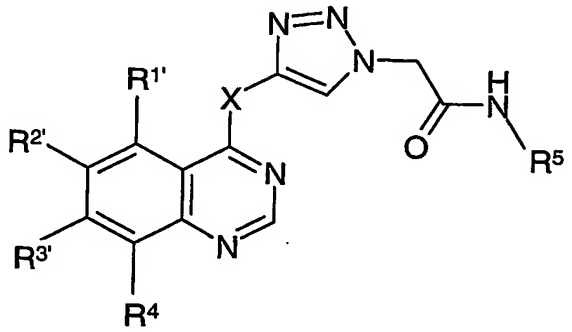
5. A compound according to claim 1 or a salt, ester or prodrug thereof wherein R^1 is hydrogen or $-OR^{11}$ and R^{11} is hydrogen, heterocyclyl selected from piperidinyl or pyrrolidinyl or C_{1-4}alkyl which C_{1-4}alkyl is optionally substituted by hydroxy, C_{1-4}alkoxy, amino, C_{1-4}alkylamino or bis(C_{1-4}alkyl)amino.

6. A compound according to claim 1 or a salt, ester or prodrug thereof wherein R^2 is hydrogen or $-OR^{12}$ and R^{12} is hydrogen, C_{1-4}alkyl, heterocyclyl or heterocyclylC_{1-4}alkyl.

7. A compound according to claim 1 or a salt, ester or prodrug thereof wherein R^3 is $-X^3R^{13}$, X^3 is $-CH_2=CH_2-$, -O- or -NH-, and R^{13} is C_{1-6}alkyl substituted by $-NR^7R^8$, heterocyclyl or halo.

8. A compound according to claim 7 or a salt, ester or prodrug thereof wherein R^7 and R^8 are independently selected from hydrogen, heterocyclyl, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, hydroxyC_{1-4}alkylC_{3-6}cycloalkyl, C_{1-4}alkoxyC_{1-4}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-4}alkyl, haloC_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyanoC_{1-4}alkyl and bis(C_{1-4}alkyl)aminoC_{1-6}alkyl; or R^7 and R^8 together with the nitrogen to which they are attached form a heterocyclic ring which ring comprises 4 to 7 ring atoms of which one is nitrogen and of which another is optionally NH or O and which ring is optionally substituted on carbon or nitrogen by a group selected from C_{1-4}alkyl, hydroxy, hydroxyC_{1-4}alkyl and hydroxyC_{1-4}alkoxyC_{1-4}alkyl, and where a ring $-CH_2-$ is optionally replaced with $-C(O)-$.

9. A compound of formula (IA)



or a salt or ester thereof

where X, X^1, X^2, X^3, R^4 and R^5 are as defined in relation to formula (I) in claim 1 and

$R^{1'}$ is hydrogen, halo, or $-X^1R^{11'}$;

$R^{11'}$ is hydrogen, phosphonooxy or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl which group is optionally substituted by 1 or 2 substituents independently selected from halo, hydroxy, phosphonooxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkyl, $-NR^{9'}R^{10'}$, $-C(O)R^{9'}$, $-C(O)NR^{9'}R^{10'}$ and $-C(O)OR^{9'}$;

$R^{2'}$ is hydrogen, halo, nitro, cyano or $-X^2R^{12'}$;

$R^{12'}$ is hydrogen, phosphonooxy or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, aryl, arylC_{1-4}alkyl, arylC_{2-4}alkenyl, arylC_{2-4}alkynyl,

heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl, which group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, hydroxy, phosphonooxy, C_{1-4}alkyl, C_{1-4}alkoxy, $-NR^{15'}R^{16'}$, $-NHC(O)NR^{15'}R^{16'}$, $-C(O)R^{15'}$ and $-C(O)OR^{15'}$;

$R^{3'}$ is hydrogen, halo or $-X^3R^{13'}$;

$R^{13'}$ is hydrogen, phosphonooxy or a group selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, aryl, arylC_{1-4}alkyl, arylC_{2-4}alkenyl, arylC_{2-4}alkynyl, heterocyclyl, heterocyclylC_{1-4}alkyl, heterocyclylC_{2-4}alkenyl and heterocyclylC_{2-4}alkynyl which group is optionally substituted by 1 or 2 substituents independently selected from $-NR^{7'}R^{8'}$, $-C(O)NR^{7'}R^{8'}$, halo, hydroxy, phosphonooxy, C_{1-4}alkyl, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkyl, hydroxyC_{1-4}alkylcarbonyl, phosphonooxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl;

$R^{7'}$ and $R^{8'}$ are independently selected from hydrogen, heterocyclyl, heterocyclylC_{1-4}alkyl, C_{1-4}alkylheterocyclylC_{1-4}alkyl, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, phosphonooxyC_{1-6}alkyl, C_{1-4}alkoxyC_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{3-6}cycloalkyl, phosphonooxyC_{3-6}cycloalkyl, hydroxyC_{1-4}alkylC_{3-6}cycloalkyl, phosphonooxyC_{1-4}alkylC_{3-6}cycloalkyl, hydroxyC_{3-6}cycloalkylC_{1-4}alkyl, phosphonooxyC_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{1-4}alkylC_{3-6}cycloalkylC_{1-4}alkyl, phosphonooxyC_{1-4}alkylC_{3-6}cycloalkylC_{1-4}alkyl, C_{1-4}alkoxyC_{3-6}cycloalkyl, C_{1-4}alkoxyC_{3-6}cycloalkylC_{1-4}alkyl, haloC_{1-6}alkyl, haloC_{3-6}cycloalkyl, haloC_{3-6}cycloalkylC_{1-4}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, cyanoC_{1-4}alkyl, aminoC_{1-6}alkyl, C_{1-4}alkylaminoC_{1-6}alkyl, bis(C_{1-4}alkyl)aminoC_{1-6}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkylcarbonyl, phosphonooxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl;

or $R^{7'}$ and $R^{8'}$ together with the nitrogen to which they are attached form a heterocyclic ring which ring is monocyclic or bicyclic and comprises 4 to 7 ring atoms of which one is nitrogen and of which another is optionally selected from N, NH, O, S, SO and SO_2, and which ring is optionally substituted on carbon or nitrogen by 1 or 2 substituents independently selected from C_{1-4}alkyl, hydroxy, phosphonooxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkoxyC_{1-4}alkyl,

C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkylcarbonyl, phosphonooxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl, and where a ring $-CH_2-$ is optionally replaced with $-C(O)-$;

$\mathbf{R^{9'}}$, $\mathbf{R^{10'}}$, $\mathbf{R^{15'}}$ and $\mathbf{R^{16'}}$ are independently selected from hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkylC_{1-4}alkyl, hydroxyC_{1-6}alkyl, phosphonooxyC_{1-6}alkyl, haloC_{1-6}alkyl, aminoC_{1-6}alkyl, C_{1-4}alkylaminoC_{1-6}alkyl and bis(C_{1-4}alkyl)aminoC_{1-6}alkyl;

or $\mathbf{R^{9'}}$ and $\mathbf{R^{10'}}$ together with the nitrogen to which they are attached form a heterocyclic ring which ring is monocyclic or bicyclic and comprises 4 to 7 ring atoms of which one is nitrogen and of which another is optionally selected from N, NH, O, S, SO and SO_2, and which ring is optionally substituted on carbon or nitrogen by 1 or 2 substituents independently selected from C_{1-4}alkyl, hydroxy, phosphonooxy, C_{1-4}alkoxy, hydroxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkoxyC_{1-4}alkyl, phosphonooxyC_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkylcarbonyl, phosphonooxyC_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyl, aminoC_{1-4}alkylcarbonyl, C_{1-4}alkylaminoC_{1-4}alkylcarbonyl and bis(C_{1-4}alkyl)aminoC_{1-4}alkylcarbonyl, and where a ring $-CH_2-$ is optionally replaced with $-C(O)-$;

provided that a compound of formula (IA) contains at least one phosphonooxy group.

10. A compound according to claim 9 or a salt or ester thereof wherein the compound or salt or ester thereof contains only one phosphonooxy group.

11. A compound according to claim 9 or a salt or ester thereof wherein X is NH.

12. A compound according to claim 9 or a salt or ester thereof wherein R^4 is hydrogen.

13. A compound according to claim 9 or a salt or ester thereof wherein R^5 is aryl optionally substituted by 1 or 2 halo.

14. A pharmaceutical composition comprising a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt, ester or prodrug thereof, or a compound of

formula (IA) as defined in claim 9 or a pharmaceutically acceptable salt or ester thereof in association with a pharmaceutically acceptable diluent or carrier.

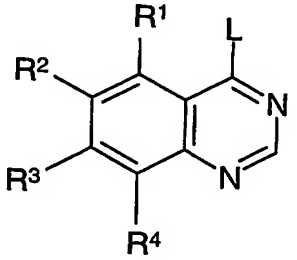
15. A compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt, ester or prodrug or a compound of formula (IA) as defined in claim 9 or a pharmaceutically acceptable salt or ester thereof for use in therapy.

16. The use of a compound of formula (I) as defined in claim 1 or a pharmaceutically acceptable salt, ester or prodrug or a compound of formula (IA) as defined in claim 9 or a pharmaceutically acceptable salt or ester thereof in the preparation of a medicament for the treatment of a hyperproliferative disease such as cancer.

17. The use as defined in claim 16 wherein the cancer is colorectal, breast, lung, prostate, bladder, renal or pancreatic cancer or leukaemia or lymphoma.

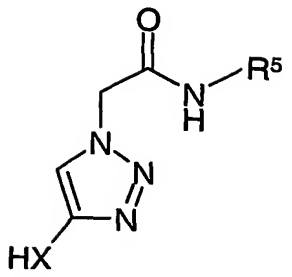
18. A method of treating a human suffering from a hyperproliferative disease such as cancer comprising the steps of administering to a person in need thereof a therapeutically effective amount of a compound of formula (I) as claimed in claim 1 or a pharmaceutically acceptable salt, ester or prodrug thereof or a compound of formula (IA) as claimed in claim 9 or a pharmaceutically acceptable salt or ester thereof.

19. A process for the preparation of a compound of formula (I) as defined in claim 1 or a salt, ester or prodrug thereof, which process comprises reacting a compound of formula (II) wherein R^1, R^2, R^3 and R^4 are as defined in claim 1



(II)

where L is a suitable leaving group with a compound of formula (III) wherein R^5 and X are as defined in claim 1



(III)

in the presence of hydrochloric acid in dioxane under an inert atmosphere,

and thereafter if necessary:

i) converting a compound of the formula (I) into another compound of the formula (I); and/or

ii) removing any protecting groups; and/or

iii) forming a salt, ester or prodrug thereof.

20. A process for the preparation of a compound of formula (IA) as defined in claim 9 or a salt or ester thereof, which process comprises phosphorylation of a suitable compound of formula (I) followed by deprotection of the phosphate group.